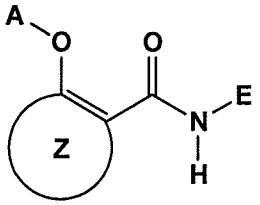
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (Currently Amended): A ~~medicament having inhibitory activity against~~ method of inhibiting NF-κB activation in a mammal, which comprises administering to a mammal an effective dose of ~~as an active ingredient~~ a substance selected from the group consisting of a compound represented by the following general formula (I) and a pharmacologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:



(I)

wherein A represents hydrogen atom or acetyl group,

E represents

a 2,5-di-substituted ~~or~~ phenyl group wherein at least one of said substituents is trifluoromethyl group,

a 3,5-di-substituted phenyl group wherein at least one of said substituents is trifluoromethyl group, or

~~a monocyclic or a fused polycyclic heteroaryl group which may be substituted,~~

~~provided that the compound wherein said heteroaryl group is (1) a fused polycyclic heteroaryl group wherein the ring which binds directly to =CONH= group in the formula (I) is a benzene ring, (2) unsubstituted thiazol-2-yl group, or (3) unsubstituted benzothiazol-2-yl group is excluded,~~

a 2-thiazolyl group which is substituted with one or more substituents selected from the group consisting of

a halogen atom,

an alkyl group which may be substituted with one or more substituents selected from the group consisting of

a carboxy group and

an alkoxy-carbonyl group,

a halogenated alkyl group,

a cyano group,

an aryl group which may be substituted with one or more substituents selected from the group consisting of

a halogen atom,

a halogenated alkyl group and

an alkoxy group,

an alkyl-carbonyl group,

an alkoxy-carbonyl group,

a monocyclic non-aromatic heterocyclic group which may be substituted with one or more substituents selected from the group consisting of

an alkyl group and

an aryl group,

an aralkyl group,

an aryl-carbonyl group,

a carbamoyl group which may be substituted with one or more substituents selected from the group consisting of

an alkyl group and

an aralkyl group, and

a carboxy group,

ring Z represents ~~an arene~~ a benzene ring which may have one or more substituents selected from the group consisting of

a halogen atom,

a nitro group,

a cyano group,

a hydroxy group,

an alkoxy group,

an alkyl group which may be substituted with one or more substituents selected from the group consisting of

a hydroxy group,

an aralkyl-oxy-imino group and

an alkoxy-imino group,

an alkenyl group which may be substituted with one or more substituents selected from the group consisting of

an aryl group,

a cyano group,

an alkoxy-carbonyl group and

a carboxy group,

an alkynyl group which may be substituted with one or more substituents selected from the group consisting of

an aryl group and

a tri(alkyl)silyl group,

a halogenated alkyl group,

an aryl group which may be substituted with one or more substituents selected from the group consisting of

a halogen atom and

a halogenated alkyl group,

an aralkyl group,

a monocyclic or a fused polycyclic heteroaryl group which may be substituted with one or more alkyl groups,

an alkyl-carbonyl group,

a monocyclic non-aromatic heterocyclic-carbonyl group which may be substituted with one or more aralkyl groups,

a monocyclic heteroaryl-sulfonyl group,

a carboxy group,

an alkoxy-carbonyl group,

a carbamoyl group which may be substituted with one or more substituents selected from the group consisting of

an aryl group which may be substituted with one or more halogenated alkyl groups and

an alkyl group,

a sulfamoyl group which may be substituted with one or more substituents selected from the group consisting of

an aryl group which may be substituted with one or more halogenated alkyl groups and

an alkyl group,

an amino group which may be substituted with one or more substituents selected from the group consisting of

an alkyl group,

an alkyl-carbonyl group,

an aryl-carbonyl group,

an alkyl-sulfonyl group and

an aryl-sulfonyl group,

an ureido group which may be substituted with one or more aryl groups,

a thioureido group which may be substituted with one or more aryl groups, and

a diazenyl group which may be substituted with one or more aryl groups wherein said aryl groups may be substituted with one or more substituents selected from the group consisting of

a nitro group and

a monocyclic heteroaryl-sulfamoyl group,

in addition to the group represented by formula –O–A wherein A has the same meaning as that defined above and the group represented by formula –CONH–E wherein E has the same meaning as that defined above, ~~or a heteroarene which may have one or more substituents in~~

~~addition to the group represented by formula -O-A wherein A has the same meaning as that defined above and the group represented by formula -CONH-E wherein E has the same meaning as that defined above~~.

2-11. (Canceled)

12. (Currently Amended): ~~The medicament according to claim 1, which is an inhibitor against~~ A method of inhibiting expression of a gene for one or more substances selected from the following substance group δ: in a mammal, which comprises administering an effective dose of a substance according to claim 1, [Substance group δ] tumor necrosis factor (TNF), interleukin-1, interleukin-2, interleukin-6, interleukin-8, granulocyte colony-stimulating factor, interferon β, cell ~~adhension~~ adhesion factor ICAM-1, VCAM-1, ELAM-1, ~~nitricoxide~~ nitric oxide synthetase, major histocompatibility antigen family class I, major histocompatibility antigen family class II, β2-microglobulin, immunoglobulin light chain, serum amyloid A, angiotensinogen, complement B, complement C4, c-myc, transcript derived from HIV gene, transcript derived from HTLV gene, transcript derived from simian virus 40 gene, transcript derived from cytomegalovirus gene, and transcript derived from adenovirus gene.

13. (Currently Amended): ~~The medicament according to claim 1, which is an inhibitor against~~ A method of inhibiting production and release of an inflammatory cytokine or ~~an immuno suppressive agent~~ of immune inhibition in a mammal, which comprises administering to a mammal an effective dose of a substance according to claim 1.

14. (Currently Amended): ~~The medicament according to claim 1, which is used for preventive and/or therapeutic treatment of~~ A method of treating chronic rheumatism in a mammal, which comprises administering to a mammal an effective dose of a substance according to claim 1.

15. (New): The method according to claim 1, wherein E is a 2,5-di-substituted phenyl group wherein at least one of said substituents is trifluoromethyl group.

16. (New): The method according to claim 15, wherein E is a 2,5-di-substituted phenyl group wherein at least one of said substituents is trifluoromethyl group, and the other substituent is selected from the group consisting of

a halogen atom,

a halogenated alkyl group,

a nitro group,

an alkyl group,

an alkoxy group,

an alkyl-sulfanyl group,

a monocyclic non-aromatic heterocyclic group which may be substituted with one or more halogenated alkyl groups,

an aryl-oxy group which may be substituted with one or more substituents selected from the group consisting of

a halogen atom,

an alkoxy group,

an alkyl group and

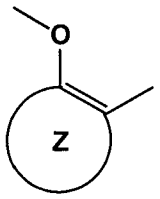
a cyano group, and

a halogenated alkoxy group.

17. (New): The method according to claim 16, wherein E is a 2-chloro-5-(trifluoromethyl)phenyl group, a 2,5-bis(trifluoromethyl)phenyl group, a 2-fluoro-5-(trifluoromethyl)phenyl group, a 2-nitro-5-(trifluoromethyl)phenyl group, a 2-methyl-5-(trifluoromethyl)phenyl group, a 2-methoxy-5-(trifluoromethyl)phenyl group, a 2-methylsulfanyl-5-(trifluoromethyl)phenyl group, a 2-(1-pyrrolidinyl)-5-(trifluoromethyl)phenyl group, a 2-morpholino-5-(trifluoromethyl)phenyl group, a 2-bromo-5-(trifluoromethyl)phenyl group, a 2-(2-naphthyloxy)-5-(trifluoromethyl)phenyl group, a 2-(2,4-dichlorophenoxy)-5-

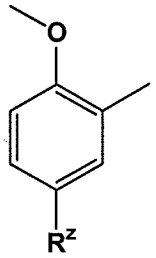
(trifluoromethyl)phenyl group, a 2-[4-(trifluoromethyl)piperidin-1-yl]-5-(trifluoromethyl)phenyl group, a 2-(2,2,2-trifluoroethoxy)-5-(trifluoromethyl)phenyl group, a 2-(2-methoxyphenoxy)-5-(trifluoromethyl)phenyl group, a 2-(4-chloro-3,5-dimethylphenoxy)-5-(trifluoromethyl)phenyl group, a 2-piperidino-5-(trifluoromethyl)phenyl group, a 2-(4-methylphenoxy)-5-(trifluoromethyl)phenyl group, a 2-(4-chlorophenoxy)-5-(trifluoromethyl)phenyl group, a 2-(4-cyanophenoxy)-5-(trifluoromethyl)phenyl group or a 2-(4-methoxyphenoxy)-5-(trifluoromethyl)phenyl group,

the following partial formula (Iz-1) in the general formula containing ring Z



(Iz－1)

is represented by the following formula (Iz-2):



(Iz－2)

wherein R^z represents a hydrogen atom, a halogen atom, a nitro group, a cyano group, a methoxy group, a methyl group, an isopropyl group, a tert-butyl group, a 1,1,3,3-tetramethylbutyl group, a 2-phenylethen-1-yl group, a 2,2-dicyanoethen-1-yl group, a 2-cyano-2-(methoxycarbonyl)ethen-1-yl group, a 2-carboxy-2-cyanoethen-1-yl group, an ethynyl group, a phenylethynyl group, a (trimethylsilyl)ethynyl group, a trifluoromethyl group, a pentafluoroethyl group, a phenyl group, a 4-(trifluoromethyl)phenyl group, a 4-fluorophenyl group, a 2,4-difluorophenyl group, a 2-phenethyl group, a 1-hydroxyethyl group, a 1-(methoxyimino)ethyl group, a 1-[(benzyloxy)imino]ethyl group, a 2-thienyl group, a 3-thienyl group, a 1-pyrrolyl group, a 2-methylthiazol-4-yl group, an imidazo[1,2-a]pyridin-2-yl group, a 2-pyridyl group, an acetyl group, an isobutyryl group, a piperidinocarbonyl group, a 4-benzylpiperidinocarbonyl group, a (pyrrol-1-yl)sulfonyl group, a carboxy group, a methoxycarbonyl group, a N-[3,5-

bis(trifluoromethyl)phenyl]carbamoyl group, a N,N-dimethylcarbamoyl group, a sulfamoyl group, a N-[3,5-bis(trifluoromethyl)phenyl]sulfamoyl group, a N,N-dimethylsulfamoyl group, amino group, a N,N-dimethylamino group, an acetylamino group, a benzoylamino group, a methanesulfonylamino group, a benzenesulfonylamino group, a 3-phenylureido group, a (3-phenyl)thioureido group, a (4-nitrophenyl)diazenyl group or a {[4-(pyridin-2-yl)sulfamoyl]phenyl}diazenyl group.

18. (New): The method according to claim 17, wherein A is a hydrogen atom, R^z is a halogen atom.

19. (New): The method according to claim 18, wherein E is a 2,5-bis(trifluoromethyl)phenyl group.

20. (New): The method according to claim 19, wherein R^z is a bromine atom.

21. (New): The method according to claim 15, wherein E is a 2,5-bis(trifluoromethyl)phenyl group.

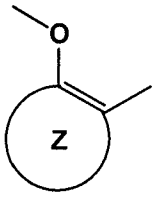
22. (New): The method according to claim 1, wherein E is a 3,5-di-substituted phenyl group wherein at least one of said substituents is trifluoromethyl group.

23. (New): The method according to claim 22, wherein E is a 3,5-di-substituted phenyl group wherein at least one of said substituents is trifluoromethyl group, and the other substituent is selected from the group consisting of

a halogenated alkyl group,
a halogen atom,
an alkoxy group,
an alkoxy-carbonyl group and
a carboxy group.

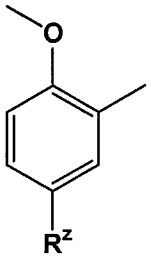
24. (New): The method according to claim 23, wherein E is a 3,5-bis(trifluoromethyl)phenyl group, a 3-fluoro-5-(trifluoromethyl)phenyl group, a 3-bromo-5-(trifluoromethyl)phenyl group, a 3-methoxy-5-(trifluoromethyl)phenyl group, a 3-methoxycarbonyl-5-(trifluoromethyl)phenyl group or a 3-carboxy-5-(trifluoromethyl)phenyl group,

the following partial formula (Iz-1) in the general formula containing ring Z



(Iz-1)

is represented by the following formula (Iz-2):



(Iz-2)

wherein R^z represents a hydrogen atom, a halogen atom, a nitro group, a cyano group, a methoxy group, a methyl group, an isopropyl group, a tert-butyl group, a 1,1,3,3-tetramethylbutyl group, a 2-phenylethen-1-yl group, a 2,2-dicyanoethen-1-yl group, a 2-cyano-2-(methoxycarbonyl)ethen-1-yl group, a 2-carboxy-2-cyanoethen-1-yl group, an ethynyl group, a phenylethynyl group, a (trimethylsilyl)ethynyl group, a trifluoromethyl group, a pentafluoroethyl group, a phenyl group, a 4-(trifluoromethyl)phenyl group, a 4-fluorophenyl group, a 2,4-difluorophenyl group, a 2-phenethyl group, a 1-hydroxyethyl group, a 1-(methoxyimino)ethyl group, a 1-[(benzyloxy)imino]ethyl group, a 2-thienyl group, a 3-thienyl group, a 1-pyrrolyl group, a 2-methylthiazol-4-yl group, an imidazo[1,2-a]pyridin-2-yl group, a 2-pyridyl group, an acetyl group, an isobutyryl group, a piperidinocarbonyl group, a 4-benzylpiperidinocarbonyl group, a (pyrrol-1-yl)sulfonyl group, a carboxy group, a methoxycarbonyl group, a N-[3,5-bis(trifluoromethyl)phenyl]carbamoyl group, a N,N-dimethylcarbamoyl group, a sulfamoyl

group, a N-[3,5-bis(trifluoromethyl)phenyl]sulfamoyl group, a N,N-dimethylsulfamoyl group, amino group, a N,N-dimethylamino group, an acetylamino group, a benzoylamino group, a methanesulfonylamino group, a benzenesulfonylamino group, a 3-phenylureido group, a (3-phenyl)thioureido group, a (4-nitrophenyl)diazenyl group or a {[4-(pyridin-2-yl)sulfamoyl]phenyl}diazenyl group.

25. (New): The method according to claim 24, wherein A is a hydrogen atom, R^z is a halogen atom.

26. (New): The method according to claim 25, wherein E is a 3,5-bis(trifluoromethyl)phenyl group.

27. (New): The method according to claim 26, wherein R^z is a chlorine atom.

28. (New): The method according to claim 22, wherein E is a 3,5-bis(trifluoromethyl)phenyl group.

29. (New): The method according to claim 1, wherein E is a 2-thiazolyl group which is substituted with one or more substituents selected from the group consisting of

a halogen atom,

an alkyl group which may be substituted with one or more substituents selected from the group consisting of

a carboxy group and

an alkoxy-carbonyl group,

a halogenated alkyl group,

a cyano group,

an aryl group which may be substituted with one or more substituents selected from the group consisting of

a halogen atom,

a halogenated alkyl group and

an alkoxy group,

an alkyl-carbonyl group,

an alkoxy-carbonyl group,

a monocyclic non-aromatic heterocyclic group which may be substituted with one or more substituents selected from the group consisting of

an alkyl group and

an aryl group,

an aralkyl group,

an aryl-carbonyl group,

a carbamoyl group which may be substituted with one or more substituents selected from the group consisting of

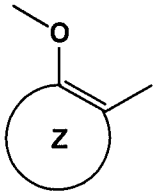
an alkyl group and

an aralkyl group, and

a carboxy group.

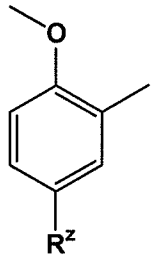
30. (New): The method according to claim 29, wherein E is a 5-bromo-4-[(1,1-dimethyl)ethyl]thiazol-2-yl group, a 5-bromo-4-(trifluoromethyl)thiazol-2-yl group, a 5-cyano-4-[(1,1-dimethyl)ethyl]thiazol-2-yl group, a 4,5-dimethylthiazol-2-yl group, a 5-methyl-4-phenylthiazol-2-yl group, a 5-(4-fluorophenyl)-4-methylthiazol-2-yl group, a 4-methyl-5-[3-(trifluoromethyl)phenyl]thiazol-2-yl group, a 4-[(1,1-dimethyl)ethyl]-5-ethylthiazol-2-yl group, a 4-ethyl-5-phenylthiazol-2-yl group, a 4-isopropyl-5-phenylthiazol-2-yl group, a 4-butyl-5-phenylthiazol-2-yl group, a 4-[(1,1-dimethyl)ethyl]-5-[(2,2-dimethyl)propionyl]thiazol-2-yl group, a 4-[(1,1-dimethyl)ethyl]-5-(ethoxycarbonyl)thiazol-2-yl group, a 4-[(1,1-dimethyl)ethyl]-5-piperidinothiazol-2-yl group, a 4-[(1,1-dimethyl)ethyl]-5-morpholinothiazol-2-yl group, a 4-[(1,1-dimethyl)ethyl]-5-(4-methylpiperazin-1-yl)thiazol-2-yl group, a 4-[(1,1-dimethyl)ethyl]-5-(4-phenylpiperazin-1-yl)thiazol-2-yl group, a 5-carboxymethyl-4-phenylthiazol-2-yl group, a 4,5-diphenylthiazol-2-yl group, a 4-benzyl-5-phenylthiazol-2-yl group, a 5-phenyl-4-(trifluoromethyl)thiazol-2-yl group, a 5-acetyl-4-phenylthiazol-2-yl group, a 5-benzoyl-4-

phenylthiazol-2-yl group, a 5-ethoxycarbonyl-4-phenylthiazol-2-yl group, a 5-ethoxycarbonyl-4-(pentafluorophenyl)thiazol-2-yl group, a 5-methylcarbamoyl-4-phenylthiazol-2-yl group, a 5-ethylcarbamoyl-4-phenylthiazol-2-yl group, a 5-isopropylcarbamoyl-4-phenylthiazol-2-yl group, a 5-(2-phenylethyl)carbamoyl-4-phenylthiazol-2-yl group, a 5-ethoxycarbonyl-4-(trifluoromethyl)thiazol-2-yl group, a 5-carboxy-4-[(1,1-dimethyl)ethyl]thiazol-2-yl group, a 5-(ethoxycarbonyl)methyl-4-phenylthiazol-2-yl group, a 5-carboxy-4-phenylthiazol-2-yl group, a 5-propylcarbamoyl-4-phenylthiazol-2-yl group, a 5-methylthiazol-2-yl group, a 4-[(1,1-dimethyl)ethyl]thiazol-2-yl group, a 4-phenylthiazol-2-yl group, a 4-[3,5-bis(trifluoromethyl)phenyl]thiazol-2-yl group, a 4-(2,4-dichlorophenyl)thiazol-2-yl group, a 4-(3,4-dichlorophenyl)thiazol-2-yl group, a 4-[4-(trifluoromethyl)phenyl]thiazol-2-yl group, a 4-(2,5-difluorophenyl)thiazol-2-yl group, a 4-(4-methoxyphenyl)thiazol-2-yl group, a 4-[3-(trifluoromethyl)phenyl]thiazol-2-yl group or a 4-(pentafluorophenyl)thiazol-2-yl group,
the following partial formula (Iz-1) in the general formula containing ring Z



(Iz-1)

is represented by the following formula (Iz-2):



(Iz-2)

wherein R^z represents a hydrogen atom, a halogen atom, a nitro group, a cyano group, a methoxy group, a methyl group, an isopropyl group, a tert-butyl group, a 1,1,3,3-tetramethylbutyl group, a 2-phenylethen-1-yl group, a 2,2-dicyanoethen-1-yl group, a 2-cyano-2-(methoxycarbonyl)ethen-1-yl group, a 2-carboxy-2-cyanoethen-1-yl group, an ethynyl group, a phenylethynyl group, a (trimethylsilyl)ethynyl group, a trifluoromethyl group, a pentafluoroethyl group, a phenyl group, a 4-(trifluoromethyl)phenyl group, a 4-fluorophenyl group, a 2,4-difluorophenyl group, a 2-

phenethyl group, a 1-hydroxyethyl group, a 1-(methoxyimino)ethyl group, a 1-[(benzyloxy)imino]ethyl group, a 2-thienyl group, a 3-thienyl group, a 1-pyrrolyl group, a 2-methylthiazol-4-yl group, an imidazo[1,2-a]pyridin-2-yl group, a 2-pyridyl group, an acetyl group, an isobutyryl group, a piperidinocarbonyl group, a 4-benzylpiperidinocarbonyl group, a (pyrrol-1-yl)sulfonyl group, a carboxy group, a methoxycarbonyl group, a N-[3,5-bis(trifluoromethyl)phenyl]carbamoyl group, a N,N-dimethylcarbamoyl group, a sulfamoyl group, a N-[3,5-bis(trifluoromethyl)phenyl]sulfamoyl group, a N,N-dimethylsulfamoyl group, amino group, a N,N-dimethylamino group, an acetylamino group, a benzoylamino group, a methanesulfonylamino group, a benzenesulfonylamino group, a 3-phenylureido group, a (3-phenyl)thioureido group, a (4-nitrophenyl)diazenyl group or a {[4-(pyridin-2-yl)sulfamoyl]phenyl}diazenyl group.

31. (New): The method according to claim 30, wherein A is a hydrogen atom, R^z is a halogen atom.

32. (New): The method according to claim 31, wherein E is a 4-[(1,1-dimethyl)ethyl]-5-[(2,2-dimethyl)propionyl]thiazol-2-yl group.

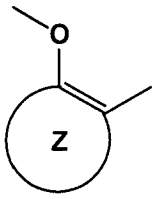
33. (New): The method according to claim 1, wherein the mammal is a human.

34. (New): The method according to claim 12, wherein the mammal is a human.

35. (New): The method according to claim 13, wherein the mammal is a human.

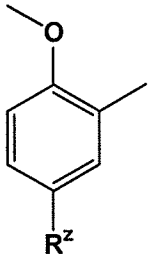
36. (New): The method according to claim 14, wherein the mammal is a human.

37. (New): The method according to claim 14, wherein A is a hydrogen atom, E is a 2,5-bis(trifluoromethyl)phenyl group,
the following partial formula (Iz-1) in the general formula containing ring Z



(I z－1)

is represented by the following formula (Iz-2):

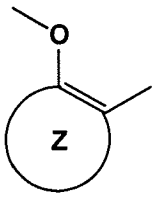


(I z－2)

wherein R^z represents a bromine atom.

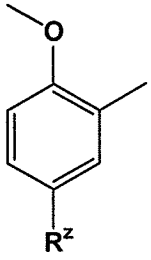
38. (New): The method according to claim 37, wherein the mammal is a human.

39. (New): The method according to claim 14, wherein A is a hydrogen atom,
E is a 3,5-bis(trifluoromethyl)phenyl group,
the following partial formula (Iz-1) in the general formula containing ring Z



(I z－1)

is represented by the following formula (Iz-2):



(I z－2)

wherein R^z represents a chlorine atom.

40. (New): The method according to claim 39, wherein the mammal is a human.